Exploring the Effect of Individual Protective Behaviors on Influenza Transmission, Using an Agent Based Model

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ABSTRACT

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Individuals develop different protective behavioral patterns toward a specific disease based on their knowledge of effective interventions. Understanding how people behave individually toward an outbreak of a disease can help experts to evaluate different control strategies and to implement the most effective one.

In this research we use the Health Belief Model (HBM) to evaluate the health behavior of students toward influenza in Concordia University and its effect on the spread of virus within the target population. We conduct a survey to gather information about the health-related attitudes and beliefs of students. We apply our survey a control and a treatment group to explore the effect of education on people's health-related behaviors patterns. Control group reflects the behavioral patterns of students based on their general knowledge of influenza and its interventions while the treatment group illustrates the level of behavioral changes after individuals have been educated by a health care expert.

In this research we use an agent-based simulation to explore the effect of individuals behaviors patterns on the spread of influenza and illustrate how the health-related behavior changes in individuals can affect the chances of exposure to the virus.

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1. Introduction

Influenza outbreaks occur every year, but the timing, severity, and duration vary from season to season. Although, fever, fatigue, aching muscles and cough are the most common consequences of catching the flu virus, serious health complications and lost work time continue to have a huge annual health and economic impact of total $87 billion/year in US. (Molinari et al., 2007) Seasonal influenza attack rates vary from 10% to 30 % in adults and 20 % to 50 % in children. (Attack rates are defined as the percentage of infected population) (Neuzil et al., 2002) An infected person can spread the influenza virus even before the symptoms appears. The constant genetic changes of influenza virus raise the possibility that an outbreak could appear. This, combined with the easy transmission of the virus, illustrates the need to control the health impact of seasonal influenza outbreaks.

A hallmark of educational experience is the frequent interactions between students. These interactions can lead to a high attack rate not only in school but also a higher secondary attack rate in both student and teacher households. Occurrence of outbreak in schools causes a significant increase in student health center visits, medication usage, absenteeism and work loss. (Dalton CB et al., 2008) Given their high attack rates, schools are an ideal place for the development of interventions and health promotion programs to prevent influenza outbreak, which can lead to an increase in community immunization coverage (Heymann et al., 2004). Delivering such programs in schools can also alleviate many of the common barriers of community-based treatments, such as time, location, transportation and cost. (King Jr et al., 2006). Problems such as the high cost of treatment, general acceptance of disease interventions, surge capacity, vaccination capacity, timing and the limitation of information distribution and etc. are the challenges that health care officials need to overcome. (Yarmand, 2010)

The difference between pandemic and seasonal influenza is that seasonal flu is predictable and has the potential to be controllable with evidenced-based management strategies (Thompson WW et al, 2003); (Thompson WW et al., 2004) While these strategies won't get rid of the flu, better management can greatly reduce the number of individuals impacted as well as the severity and duration of illness. The best way to understand the current dynamics of seasonal flu, and more importantly to manage flu and improve outcomes is through the power of modeling and simulation. Such models may serve many functions in emergency preparedness and planning, including assisting healthcare officials in understanding the scope of problems, providing insights into the downstream effects of proposed interventions, and evaluating cost, risk, and outcomes of different diseases attacks.

The objectives of this research were to understand the effect of self- initiated behaviors of individuals to improve their protection against a disease, on transmission of influenza, and to identify the strength of understanding such behaviors to develop mitigation strategies. In this study we constructed a Health Belief Model to investigate individual perceptions of the influenza virus and identified factors that impacted student intention to develop the two main protective behaviors (vaccination and social distancing) toward influenza. This study also investigated the impact of information distribution and an educational program. An agent-based discrete event model was then developed to represent the contact network of individuals. To have a realistic estimation of the model parameters and validate the model, we need a target population. The transmission of influenza within the contact network and the corresponding outbreak was simulated in a university setting. .

We hope that the results of this research help health care officials in their decision making process about implementing educational programs to increase the rate of influenza interventions.

2. Literature Review

This chapter assesses the literature relevant to disease modeling, with emphasis placed on agent-based simulation. Then Health Belief Model and its contribution to explore protective behaviors toward various diseases are discussed,

2.1. Mathematical Modeling

Mathematical models have been developed to analyze the progress of infectious diseases in a population, estimate the key parameters such as thresholds, basic reproduction numbers and contact numbers, determine their sensitivities to changes and examine different control strategies. (Hethcote, 2000) These models help to understand the transmission characteristics of infectious diseases in a population which can lead to better approaches to decreasing the attack rates. Such models can also be helpful in designing epidemiological surveys, identifying crucial data that should be collected, general forecasting and estimating their uncertainty. (Hethcote, 2000) The origin of deterministic epidemiological models dates back to early 20th century when Hamer attempted to understand and analyze the measles epidemics by developing a discrete time model, in 1906. Hamer demonstrated the number of newly cases per unit time by considering the fraction of susceptible and infected individual in the target population. (Hamer, 1906) In 1926 Kermack and McKendrick introduced the concept of thresholds for the first time. They indicated that the fraction of infected individuals within a population must exceed a critical value (threshold) to trigger an epidemic . (Kermack, McKendrick, 1927) This value is often denoted as R_0. R_0 is defined as the number of secondary infections caused by a single primary infection. When $R_0 < 1$, each person who contracts the disease will infect less than one person before dying or recovering, so the outbreak will not occur.

When $R_0 > 1$,each person who is infected will infect more than one person, so the epidemic will spread. (Hethcote, 2000) Since then, mathematical epidemiology demonstrated an exponential growth and variety of models have been formulated, analyzed, and applied to various infectious diseases. (Hethcote, 2000)

Compartmental models are the simplest and most fundamental epidemiological models. In compartmental models, the target population is divided into different compartments based on the state of individuals toward a disease (such as Susceptible, Exposed, Infected and Recovered) and is considered to have homogenous characteristics. (Hethcote, 2000) Compartmental models were first introduced between 1900 and 1935 by R.A. Ross, W.H. Hamer, A.G. McKendrick and other researchers such as W.O. Kermack. (Brauer, 2008)

Since the development of compartmental models they have been widely used to analyze and understand the spread of various infectious diseases and the impact of different control strategies. One example is the study of 1918 pandemic influenza by Mills et al, in 2004. In this study a SEIR model was developed to estimate the reproductive number of the pandemic. (Mills et al., 2004) Another example is the study of SARS outbreak in China by Zhang et al in 2005. In this study a SEIR model was developed to assess the effectiveness of different control strategies.(Zhang et al, 2005)

2.2 Agent Based Simulation

Agent-Based Modeling and Simulation (ABMS) is a relatively new approach in modeling infectious diseases. In these simulations individuals in a population, known as “agents”, have distinct behaviors, and also social interactions with other agents, which in turn influence their behaviors. Modeling the transmission of an infectious disease using ABMS helps researchers to understand the effects of such diversity of behaviors and attributes between individuals and also the effects that interactions among agents have on the transmission of disease within the population as a whole. The first attempts to develop an agent-based pandemic simulation model were in 1976, when Elveback developed an ABS to model 1918 Pandemic Influenza. (Elveback, 1976) This study modeled the interaction of 1000 people in the community, mixed in different groups such as family, neighborhoods and schools and defined the transmission risk as a function of contact time between individuals. Age-specific transmission hazard rates were obtained from the patterns observed in the 1968 and 1957 pandemics. Behavioral changes such as contact reduction and quarantine for school children were also considered in the model. All subsequent studies that adopt an ABMS approach, or an approach that considers non-homogeneous population to model an infectious disease outbreak, have many core features of this study. Another good example of earlier agent-based models was the model developed by Halloren et al. in 2002, which estimated the effectiveness of interventions such as vaccination, in keeping the attack rate of an epidemic below a pre-defined limit in a virtual population with 2,000 agents. (Halloran et al., 2002)

Later on, ABMS approaches were extended to study both the transmission of disease and the effect of interventions within larger populations under bioterrorism attack in correspondence with real world. (M. J. Haber, 2007) (T. Das, 2008) (Longini, 2004). A good example of such simulations was EpiSimS, developed by Los Alamos National Laboratory, to simulate the spread of pandemic influenza in the Greater Los Angeles area with over 18 million agents in over half a million geographic sub-locations. The hour-by-hour contact patterns used in EpiSimS were obtained from the United States National Household Travel Survey by recording the movement of people through different locations during sampled days. EpiSims was used in several studies to explore the effect of various interventions strategies on the spread of disease. For example one study found that school closures did not have a strong effect on a pandemic's attack rate, rather than delayed the pandemic's peak. (Lee et al., 2010). Another study involving EpiSimS slowed that the combination of school closures and antiviral treatments were successful in significantly reducing the infection rate before the vaccine became available. (S. M. Mniszewski, 2008)

Another large scale simulation developed by Das et al. in 2008 with over 1.1 million agents, was also designed to help healthcare executives in developing mitigation strategies related to vaccination, prophylaxis, social distancing and hospital admission by incorporating a variety of decision factors , in the case of an epidemic. (Das et al., 2008)

One of the most crucial parameters that needs to be quantified when simulating an infectious disease is the probability of virus transmission between any infectious and susceptible person. Brankston et al. introduced four possible modes of human to human transmission for influenza:

1. Airborne aerosols: transmission happens when individuals breathe in very small particles known as aerosols, defined as ≤ 5μm in diameter. These particles are spread by coughing, speaking, or breathing, or when larger droplets evaporate.

2. Droplets: droplets are larger particles than aerosols (>5μm). Transmission occurs when droplets make direct contact with the interior (mucosa) of the nose or mouth oral. This occurs when an infected individual spreads droplets, generally by coughing , sneezing or speaking.

3.Direct contact: transmission happens when infectious and susceptible people come into direct physical contact.

4. Transmission occurs when particles (either aerosolized or droplet) land on objects and are touched by susceptible individuals. (Brankston G, 2007)

Despite vast experimental and epidemiological literature on the matter, there is no conclusive assurance on the relative importance of those modes. Consequently, it is not possible to validate how transmission risk should be quantified. (Brankston G, 2007)

Although many pandemic simulation models have been used to test various mitigation strategies, one of the characteristics of a population that usually is left out of models, is the self-initiated behaviors that individuals develop to protect themselves in an outbreak. Many psychological models have been proposed to explore the impact of human behavioral change on the spread of an infectious disease. These models could provide a relatively comprehensive understanding of the effect of psychological, social, economic and environmental factors on the individual's health behavior. .(Glantz et al. 2007) Glantz propose Health Belief Model (HBM), Theory of Reasoned, Action/Planned Behavior, Social Cognitive Theory and the Transtheoretical Model as the four most commonly used psychological models for this purpose, every one of which has proven to have its own strength on exploring different aspects of such behaviors.(Glantz et al. 2007)

2.3 Health Belief Model

HBM was first proposed by a group of social psychologists in the 1950s to explain why medical screening programs offered by the U.S. Public Health service were not very successful.(Rosenstock,1974) HBM suggests that when individuals believe that a condition is a threat to their personal health and developing a specific behavior will reduce the perceived threat, the likelihood of engaging in that behavior will increase. The following four factors are the original construction of HBM:

•Perceived Susceptibility: The level of risk the individual is in, toward that illness

•Perceived Severity: The seriousness of the consequences associated with the illness

•Perceived Benefit: The benefits of developing the protective behavior

•Perceived Barrier: The negative effects and the barriers associated with developing the protective behavior (Janz, 1984)

Since it was first developed, the HBM model has been reformulated to increase its effectiveness by incorporating psychological and social factors. Cognitive factors such as Cues to Action (strategies that increases individual willingness to develop a behavior) and Self-efficacy (individual confidence to develop the behavior) were introduced by Bandura. (Bandura, 1977) Later, the importance of self-efficacy as the required trigger for the action was acknowledged and the model was extended with self-efficacy as an additional independent variable along with the traditional ones. (Rosenstock, 1988). Together these six factors of the HBM provide a useful framework for designing behavior change strategies.

HBM has been used in many studies related to diseases such as cancer, HIV, hepatitis B, etc , to analyze the outcomes of developing interventions to minimize the adverse outcomes (Champion et al., 2008) (Lin et al., 2005) (De Wit et al., 2006). One of the most common practice area of HBM is in the field of HIV. For example a study among Asian-American college students , introduced the perceived severity and barriers to be significant predictors of developing protective behaviors such as precaution in the selection of sexual partners and reduction of the numbers of sexual partners. Another study investigated the effect of the HBM constructs on three of protective behaviors toward HIV: number of sexual partners, frequency of sexual intercourse, and consistency of condom use. The study indicated that self-efficacy was a significant predictor of all three behaviors. Perceived barrier was a significant predictor of frequency of intercourse and perceived severity was a significant predictor of frequency of condom use.(kraemer, 2006)

HBM has also been used to study beliefs and behaviors toward influenza virus vaccination. (Coe et al., 2012), (Lau et al., 2010), (Maurer et al.,2010). A study developed a school-based educational program constructed from the Health Belief Model, toward seasonal flu vaccination for a year, which led to a significant increase of vaccination rates among middle and high school students, in US. (Painter et al., 2010). Another study investigated the effect of the HBM variables on two protective behaviors toward influenza: vaccination, and avoiding the crowded places. This study indicated that all HBM variables except perceived susceptibility were significant predictors of vaccination and avoiding crowded places was correlated with only perceived benefit of this behavior. (Durham et al., 2012)

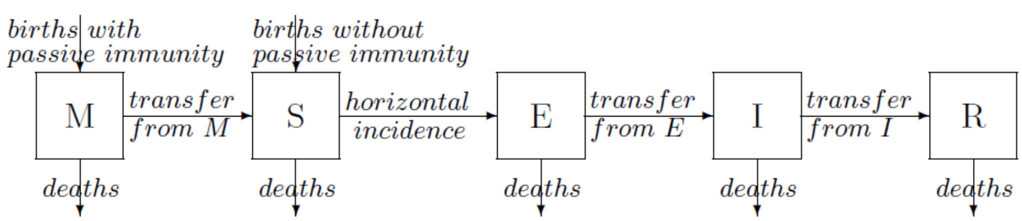
3. Modeling:

In this chapter, we present the modeling process. We start by a detailed discussion of the model development key concepts. Then we present the HBM study representation.

3.1 Compartmental Model

Compartmental model is described by the flow of individual between disease classes such as M (Maternally derived immunity), S (Susceptible), E (Exposed), I (Infectious), and R (Recovered) based on specific rates; as shown in Figure 1. (Hethcote et al., 2000) In compatmental models the population is assumed to have homogenous charactristics. (Hethcote et al., 2000)

Figure I. Transfer diagram for the MSEIR model (Hethcote et al., 2000)



From different existing acronyms such as MSEIR, MSEIRS, SEIR, SEIRS, SIR, SIRS, SEI, SEIS, SI, and SIS, SEIR model is considered to be the best approach to represent the characteristics of influenza virus. (Kraemer, 2006)

As shown in figure I, three transfer rates needs to be defined for the flow of individuals between the compartments. The first transfer rate is the "Horizontal Incidence" which determines the number of susceptible individuals that get exposed to virus per unit of time. (Hethcote, 2000). Horizontal Incidence is calculated based on the "average number of effective contacts" of a susceptible person per unit time and the fraction of infected individuals within the target population. The transfer rate between E and I compartments and the transfer rate between I and R compartments are defined as a function of number of individual in a compartment and the average of waiting time in the next compartment. (Hethcote, 2000)

The number of individuals in each of compartments are denoted by S(t), E(t), I(t) and R(t) for Suceptible, Exposed, Infected and Recovered compartments respectively. The total number of individuals in target population is denoted by N at time t which can be assessed by

$$N(t) = S(t) + E(t) + I(t) + R(t) \qquad (1)$$

The infectious fraction at time (f_I (t)) and susceptible fraction at time (f_S(t)) can be calculated by

$$f_I(t) = \frac{I(t)}{N(t)} \qquad (2)$$

$$f_S(t) = \frac{S(t)}{N(t)} \qquad (3)$$

Then if we denote the average number of effective contacts of a susceptible person per unit time by β , then the average number of contacts with infected individuals per unit time for a susceptible person is $\frac{\beta I}{N} = \beta f_I$ and $\left(\frac{\beta I}{N}\right) S = \beta N f_I f_S$ is the number of new cases per unit time. (Hethcote, 2002) As a result, if we denote the horizontal incidence at time t by H(t), then we have

$$H(t) = \beta(t)(t) f(t) \qquad (4) \text{ (Yarmand, 2011)}$$

Estimates based on research on the duration for which infected people shed virus indicate a latent period of about 1.9 days and an infectious period of 4.1 days.(Longini et al, 2004) These correspond to the average amount of time one would be in the E and I compartments of the model, respectively.

The use of an SEIR model also is efficient with the behavioral interventions likely to be used against influenza. Preventive behaviors such as vaccination, social distancing and hand washing would be targeted to susceptible people. Similarly, isolation applies only to those who are presently infected.

3.2. Model Development

We applied a discrete-event agent-based simulation to model a virtual replication of influenza outbreak in a university setting. The synthetic population was constructed to match the population of Concordia University's undergraduate engineering students at the time. Other inhabitants such as faculty, staff, visitors and graduate students were not considered in this simulation. The university was represented physically by a set of sub locations in which students were more likely to interact with each other. The locations were reasonably isolated from students of other majors. Each student moved from location to location throughout a typical day defined by their schedule. Disease related data was taken from the literature of influenza studies. The required data about student schedules, as well as the time, duration and location of each course was obtained from Concordia's Undergraduate Student Course Database. To acquire data on student activities on campus, and their health related behavior toward influenza a questionnaire survey was conducted. Information about school sub-locations geography, including seating orders was obtained from Concordia's Security Department.

3.3. Model Assumption and Parameters

3.3.1. Influenza Transmission

One of the most crucial parameters that needs to be quantified when simulating an infectious disease is the probability of virus transmission between any infected and susceptible person. There are several modes of influenza transmission, and despite vast experimental and epidemiological literature on the matter, there is no conclusive assurance on the relative importance of those modes. Consequently, it is not possible to validate how transmission risk should be quantified. (Brankston G, 2007) In agent-based models such as ours, the probability of the transmission of disease between two people in close contact over time is typically assumed to be captured with a hazard rate. (Brankston G, 2007) Although this hazard rate could vary according to factors such as temperature, humidity, ventilation individual susceptibility, etc., it is not unreasonable to consider an average population hazard rate for influenza transmission.(Haber et al, 2007) In addition, these infectious contacts are believed to occur only within a specific radius of the infectious person (Brankston G, 2007) Table I illustrates the probability that such contact between a susceptible individual and an infectious one lead to exposure to the virus, obtained using per minute hazard rates estimated by Haber et al.(Haber et al, 2007) As show in Table I the probability for the contacts between two adults is λ= 0.00032. The probability that a susceptible individual becomes infected during a physical contact within a specific radios (1.888 meters for influenza), can be calculated by a transmission probability of per minute contact with any infectious individual that one comes into contact with:

$$P(infection) = 1 - e^{-\lambda t} \qquad (5)$$

Since the number of people at a location at any time varies widely, once a susceptible person arrives to a location, s/he may come in contact with more than one infectious person at a time. Therefore in this simulation once a susceptible person decided to leave a sub location in the model the probability of infection was calculated based on the period of contact for all the infectious contacts s/he made in that sub location:

$$P(infection) = 1 - e^{-\lambda(t_1 + t_2 + \cdots)} \qquad (6)$$

Table I: Transmission rates (λ_{ij}) from an infected person in age group j to a susceptible person in age group i. (Haber et al, 2007)

	Age group of susceptible			
Age group of infected	0–4	5–18	19–64	>65
0–4	0.00059	0.00062	0.00033	0.00080
5–18	0.00058	0.00061	0.00033	0.00080
19–64	0.00057	0.00053	0.00032	0.00080
>65	0.00057	0.00054	0.00029	0.00102

Once an individual left the school, the probability that transmission occurred during their absence was calculated for each susceptible person, based on the average number of contacts made in their community or household, using the estimated duration of contacts and number of contacts in the household or community by a susceptible person with age between 19-64.

Table II: Average duration of contacts with household members per minutes. (Haber et al, 2007)

	Age group of susceptible			
Age group of infected	0–4	5–18	19–64	>65
0–4	120	60	120	60
5–18	60	120	120	60
19–64	120	120	120	120
>65	60	60	120	120

Table III: Number of contacted persons and total duration of all contacts with 1 person in the community. (Haber et al, 2007)

	Age group of susceptible (i)			
Age group of infected (j)	0–4	5–18	19–64	>65
0–4	2,60	1,30	0	0
5–18	1,30	2,60	0	0
19–64	0	0	2,60	2,60
>65	0	0	120	2,60

3.3.2 Disease Parameters

In this simulation once a susceptible person was exposed to the virus, s/he entered into latent and incubation stages followed by a symptomatic or asymptomatic infectious period. During the latent period the individual was infected but not yet able to transmit the virus. The incubation period, was considered to be one day longer than the latent period for the influenza virus and was the period between the exposure to the virus and the onset of symptoms of the disease. After the infectious period finished the individual recovered from the disease and stayed immune to virus for the rest of the flu season.

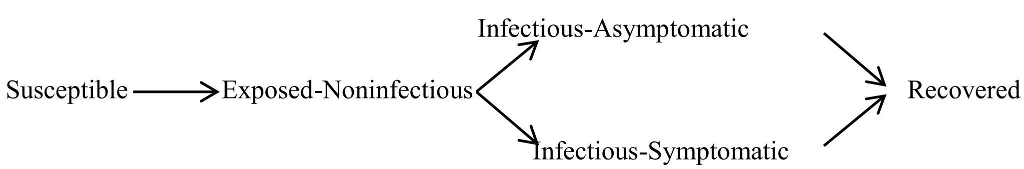
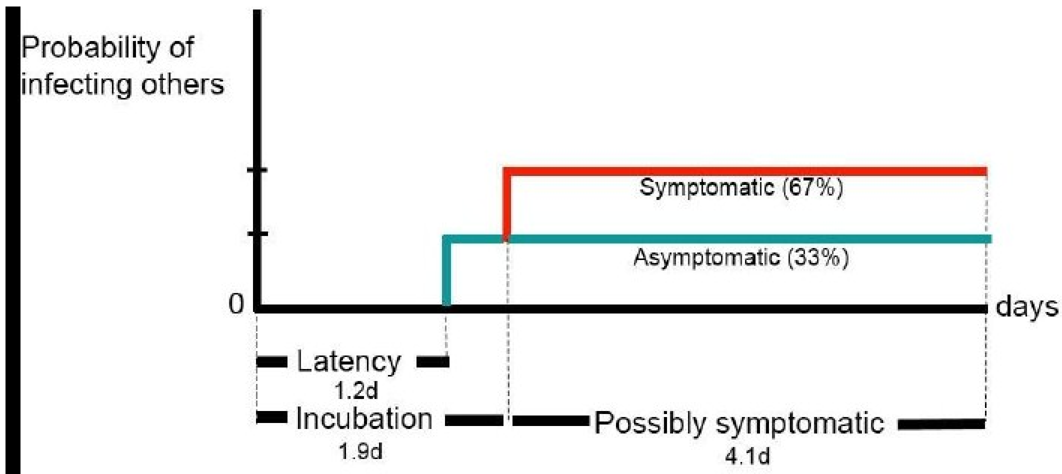


Figure II: Disease stages in simulation

Estimated distributions for the latent and infectious periods used in this simulation were obtained from Elveback et al. Each individual was assigned a health status attribute at time which was associated with one of following timelines: susceptible, exposed-noninfectious (latent period), infectious-asymptomatic, infectious-symptomatic and recovered. (Elveback etal.,1976) We assumed that the probability of developing symptoms, given influenza infection, was 0.67 and that an infected person who did not become ill was 50% less infectious than one who did, but the incubation and infectious period durations is the same as those cases that do exhibit symptoms. (Longini, 2005) Figure III displays the periods and parameter values used in model.



	Incubation (latent) period			Possibly symptomatic period			
Number of days	1 (1)	2 (1)	3 (2)	3	4	5	6
Probability (all ages)	0.3	0.5	0.2	0.3	0.4	0.2	0.1

Figure III : Influenza Parameters. (Longini, 2005)

3.3.3 Influenza Interventions and Individual Behavior

In the event of a disease outbreak with a high attack rate in a population, it is likely that much of the behavioral control would be done through personal protective behavior, such as vaccination or social distancing. These behaviors are likely to be important control measures for those people who are susceptible to disease and could have a significant impact on the transmission of disease. It is believed that decreasing the amount of contact between infected and susceptible individuals by encouraging them to avoid crowded places or close physical contact with each other could slow the outbreak and lower its peak, (Bell DM, 2006) (Heymann A, 2004). For instance in the 1918 influenza pandemic, people avoided places where they might come into contact with others, out of fear that close contacts would expose them to greater risk of infection and that staying home would protect them from illness. (Barry, 2004)

In this study we constructed a Health Belief Model to investigate individual perceptions of the influenza virus and identified factors that impacted student intention to develop the two main protective behaviors (vaccination and social distancing) toward influenza. This study also investigated the impact of information distribution and an educational program. Results gained from this study about participants perception were used to debates probabilities of social distancing and vaccination for each individual incorporated into simulation as the health-behavior pattern. This cross-sectional study was conducted in Concordia University. Students from the Faculty of Engineering and Computer Science undergraduate population were targeted for participation in this study due to accessibility, expense, and time considerations. Background information of participants such as age and education were not considered in the study because of the generally homogenous characteristics of the target population.

3.4. Health Belief Model (HBM)

3.4.1. Theoretical Framework

Psychologists have developed many models to explain individuals' attitudes and beliefs toward their health and how to implement educational strategies to change their health behaviors. Such models are known as value-expectancy theories which are based on the idea that individuals expect specific outcomes for their actions. (Hilyer, Veasey, Oldfield, & McCormick, 1999) HBM is one of the most well-known value-expectancy theories that emphasize on two variables: 1) the value an individual places on a specific outcome and 2) the likelihood that individual considers for a behavior to result in that outcome. As discussed before, The following factors are the construction of HBM:

- Perceived Susceptibility
- Perceived Severity
- Perceived Benefit
- Perceived Barrier (Janz, 1984)

Perceived susceptibility measures the level of vulnerability or risk that one feels toward an illness. Perceived susceptibility measures the level of seriousness of consequences (both medical and social) that one considers for contracting an illness. Both perceived susceptibility and perceived severity provide an individual with motivation to act. (Rosenstock, 1974) Perceived benefits illustrate the individual' perception of feasibility and effectiveness of a specific behavior or intervention to reduce the threat of an illness. Perceived barriers illustrate individual perception of adverse effects of an action such as its cost, side effects, inconveniency, time-consuming and etc. (Janz, 1984)

Behavior during an epidemic is best modeled using the four core constructs of the Health Belief Model: perceived susceptibility, perceived severity, perceived benefits and perceived barriers (Kraemer, 2006)

3.4.2. Survey Instrument

In this study social distancing and vaccination were considered as the protective behaviors individuals could develop toward the influenza virus.

In order to consider all the possible perceived barriers and benefits of each interventions that individuals might have and possible perceptions toward influenza which could be defined as their perceived severity and susceptibility, we included 2 or 3 questions for each domain

A 25-item questionnaire was developed to assess the study objectives. The first portion of the questionnaire contained of 20 questions, separated into a five-point Likert scale (1 = strongly disagree to 5 = strongly agree) based on HBM variables (perceived susceptibility and severity toward influenza and the perceived benefits and barrier of its interventions). The second portion of the questionnaire contained questions investigating students' history for applying the interventions, (3 items) and questions based on cues to action variable (2 Items). (See Appendix III for more information)

3.4.3. Data Collection

The survey was initially administered in two different sections of the same engineering course. The first survey administered was a control. The second survey administered involved a treatment consisting of a health promotion specialist talking to students about influenza and its interventions for 20 minutes. The educational program focused on the core HBM variables: Susceptibility of people to influenza virus, severity of influenza, benefits and barriers of Vaccination, benefits and barriers of social distancing. Since the second survey was administered on the day of an exam, there were significantly more students in attendance. In order to better compare the impacts of the treatment with the control, we collected 60 additional surveys at the university library. We conducted a two-sided mean difference t-test to confirm that the surveys collected in class and at the library were substantially similar to one another. This analysis is included below.

3.4.4. Data Analysis

Data were analyzed using SPSS/PC software Version 13.0. In this section we describe the methodology used to analyze the survey results. Descriptive statistics including mean and standard deviation were calculated for all variables. Descriptive statistics were helpful in generally describing the HBM variables.

In the second step, the HBM-based questions were clustered according to domains (perceived susceptibility to the virus, perceived severity of the virus, perceived benefits of interventions and the perceived barriers of interventions). A two-sided mean difference t-test was conducted for all questions to measure the effect of treatment. HBM variables assessed with more than one question required a measure of internal consistency. Cronbach's alpha was calculated for the perceived susceptibility of influenza with three questions in its domain. Item demonstrating low correlation with their respective scales were deleted and internal consistency was recomputed by SPSS. Pearson's correlation was used for the domain with two items. A scaled mean was calculated for domains with an alpha coefficient or Pearson correlation > 0.5.

Bivariate logistic regression was used to assess the relationship between health belief model domains and influenza interventions. Response categories for the 17 HBM questions was put into binary categories: either low (the five-point items between levels 1–2) or high (those between levels 3-5). "No interventions" were considered as the reference categories and p-values less than 0.05 were considered as statistically significant. (See Appendix I for more information on bivariate logistic regression)

Finally, a multivariate logistic regression analysis was performed to construct the logistic regression Health Belief Model and to identify significant predictors of the target preventive behavior Table VI. Odds ratios (ORs) for each predictor were estimated from the logistic regression. (See Appendix II for more information on Multivariate logistic regression)

3.4.5. Results

Demographic information and intervention history

Of the 240 students who responded to the survey, 57% were male and 43% were female. An increase in participant vaccination rate was observed in the population compared to previous years. Approximately 28% of students had influenza vaccination experience in the past and 32% were vaccinated in the current year. 14% of students had a member of a high risk influenza group in their household. 67% of students with a high risk member in their household were vaccinated against influenza. Approximately 62% of students applied social distancing in their daily contacts with others and 52% of students with high risk members in their household applied social distancing.

Health Belief Model variables

Table IV displays the results of the internal reliability test. All the questions passed the reliability test within their target domains (Cronbach's alpha for perceived susceptibility and Pearson correlations for other domains are > 0.5)

Table IV also displays a summary of the scaled means and standard deviations of each of the HBM variables in the survey. We conducted the t-test to determine if there is a significant difference between HBM variables of control groups and the treatment group. Subjects in the treatment group demonstrate a significant difference at the 0.05 α level for the mean values of perceived susceptibility, perceived barrier to vaccination and the perceived benefit of social distancing.

Table IV: Summary of Health Belief Model responses of survey participants

Items	***Control Group*** *(n=120)*		***Treatment Group Session****(n=140)*	
HBM Variables	***Mean(SD)***	***Alpha***	***Mean(SD)***	***Alpha***
Perceived Susceptibility:				
1- If I get the influenza virus, I will get sick.	*3.07(0.76)*	*0.67*	*3.87(0.82)**	*0.72*
2- I am at risk of getting the influenza virus by going to the university.				
3- My family members are at risk of getting the influenza virus.				
Scaled 1 to 5, for strongly disagree, disagree, neutral, agree, strongly agree				
Perceived Severity:				
1- If I get the influenza virus, it will disrupt my studies.	*3.02(0.79)*	*0.61*	*3.12(0.89)*	*0.59*
2- If I get the influenza virus, others in my home will get sick.				
Scaled 1 to 5, for strongly disagree, disagree, neutral, agree, strongly agree				
Vaccination Perceived Benefits				
1- If I get the influenza vaccine, I will not get sick from the influenza virus.	*3.05(0.72)*		*3.16(0.63)*	
Scaled 1 to 5, for strongly disagree, disagree, neutral, agree, strongly agree				
Vaccination Perceived Barriers				
1- If I get the influenza vaccine, I will have side effects.	*3.87(0.8)*	*0.63*	*2.33(0.88)***	*0.57*
2- It is inconvenient to get the influenza vaccine.				
Scaled 1 to 5, for strongly disagree, disagree, neutral, agree, strongly agree				
Self- Isolation Perceived Benefits				
1- I will recover faster if I rest at home as soon as influenza symptoms develop.	*3.72(0.92)*		*3.78(0.93)*	
Scaled 1 to 5, for strongly disagree, disagree, neutral, agree, strongly agree				
Self- Isolation Perceived Barriers				
1- Staying at home when I am sick has a negative effect on my studies.	*3.97(0.85)*	*0.83*	*3.51(0.62)*	*0.71*
2- My professors do not consider illness as an excusable reason for absence.				
Scaled 1 to 5, for strongly disagree, disagree, neutral, agree, strongly agree				
Physical Distancing Perceived Benefit				
1- Avoiding crowded places reduces my likelihood of catching influenza.	*3.51(0.78)*	*0.69*	*4.23(0.89)**	*0.61*
2- Avoiding physical contact with sick people reduces my likelihood of catching influenza				
Scaled 1 to 5, for strongly disagree, disagree, neutral, agree, strongly agree				
Physical Distancing Perceived Barriers				
1- It is difficult to avoid close physical contact with my friends when I am sick.	*3.72(0.79)*	*0.73*	*3.78(1.12)*	*0.54*
2- It is difficult to avoid crowded places at the university.				
Scaled 1 to 5, for strongly disagree, disagree, neutral, agree, strongly agree				

The significance of differences between answers of control and treatment group, are indicated:*for $p \leq 0.05$,** for $p \leq 0$.

Vaccination in respect to Core HBM variables

The bivariate logistic regression results are summarized in Table V. Results of regression for the surveys of control group, indicated that vaccination is highly correlated with perceived severity of influenza (*2.23 odds ratio)* and also perceived benefit (*2.1 odds ratio).* This means that an individual with a high perceived severity of influenza and low perceived barriers, benefits and susceptibility is 2.2 times more likely to vaccinate than an individual with a low perception of all HBM variables. Perceived barrier to vaccination was also highly correlated with the decision to vaccinate; those who perceived high barriers to vaccination were half as likely to vaccinate as those who perceived low barriers, all other HBM variables being equal. (*0.55 odds ratio)*. There is no significant correlation between the perceived susceptibility of disease and vaccination. Results of regression for the surveys treatment group (with the information session) indicated that vaccination is highly correlated with all the HBM variables but particularly between vaccination and the perceived benefits of this behavior (*2.25 odds ratio).*

The multivariate logistic regression results are summarized in Table VI. Results of regression for the control indicate that all of HBM variables are correlated with vaccination, but perceived severity of disease is not significant. Results of multivariate regression for the treatment group indicated that vaccination is highly correlated with all the HBM variables.

Table V: Bivariate regression of HBM variables attitudinal variables and influenza interventions

	Vaccination				*Self-Isolation*				*Physical distancing*			
	Control		*Treatment*		*Control*		*Treatment*		*Control*		*Treatment*	
	Odds Ratio	*P-Value*	*Odds ratio*	*P-Value*	*Odds Ratio*	*P-value*	*Odds Ratio*	*P-Value*	*Odds Ratio*	*P-Value*	*Odds Ratio*	*P-Value*
Perceived Susceptibility:												
Strongly agree, agree,neutral	*1*		*1*		*1*		*1*				*1*	
Strongly disagree, disagree	*2.233*	*0.021**	*2.41*	*0.041**	*1.272*	*0.0177*	*3.420*	*0.048*	*n.s.*		*1.783*	*0.032**
Perceived Severity:												
Strongly agree, agree, neutral	*1*		*1*		*1*		*1*		*1*		*1*	
Strongly disagree, disagree	*1.97*	*0.063*	*2.061*	*0.037**	*2.318*	*0.0021**	*1.573*	*0.44*	*1.967*	*0.086*	*1.921*	*0.029**
Vaccination Perceived Benefits												
Strongly agree, agree, neutral	*1*		*1*									
Strongly disagree, disagree	*2.087*	*0.006**	*2.254*	*0.009***	*n.a.*		*n.a.*		*n.a.*		*n.a*	
Vaccination Perceived Barriers												
Strongly agree, agree, neutral	*1*		*1*									
Strongly disagree, disagree	*0.553*	*0.034**	*0.675*	*0.016**	*n.a.*		*n.a.*		*n.a.*		*n.a.*	
Self- Isolation Perceived Benefits												
Strongly agree, agree, neutral					*1*		*1*					
Strongly disagree, disagree	*n.a.*		*n.a.*		*1.485*	*0.095*	*1.862*	*0.080*	*n.a.*		*n.a.*	
Self- Isolation Perceived Barriers												
Strongly agree, agree, neutral					*1*		*1*					
Strongly disagree, disagree	*n.a.*		*n.a.*		*0.433*	*0.037**	*0.44*	*0.0004*	*n.a.*		*n.a.*	
Physical Distancing Perceived Benefit												
Strongly agree, agree, neutral									*1*		*1*	
Strongly disagree, disagree	*n.a.*		*n.a.*		*n.a.*		*n.a.*		*2.683*	*0.039**	*3.789*	*0.0007*
Physical Distancing Perceived Barriers												
Strongly agree, agree, neutral									*1*		*1*	
Strongly disagree, disagree	*n.a.*		*n.a.*		*n.a.*		*n.a.*		*0.64*	*0.022**	*0.87*	*0.29*

Notes:* p≤0.05,**p≤0.01,***p≤0.001. NA (Not Applicable), NS (Not Significant at p≤0.05

Self-Isolation in respect to Core HBM variables

Bivariate logistic regression for the control group indicated that self-isolation is highly correlated with the perceived severity of influenza (OR=*2.318)* and the perceived severity of influenza (OR=2.22). Additionally, individuals who perceived barriers to self-isolation, were significantly less likely to consider self-isolation (OR=*0.433)*. There is no significant correlation between self-isolation and the perceived benefits of this behavior. Results for the treatment group indicated that self-isolation is highly correlated with the perceived susceptibility of disease (OR=*3.420)* and the perceived barriers of self-isolation (OR=*3.420)*. There is no significant correlation between self-isolation and other HBM variables.

The multivariate logistic regression results are summarized in Table VI. Results of regression for the control group indicate that all of HBM variables are correlated with self-isolation, but the perceived benefit of self-isolation is not significant. Regression results for the treatment group indicate that perceived susceptibility, benefits and barriers are correlated with self-isolation, but the perceived benefit of self-isolation and perceived severity of influenza are not correlated.

Physical- Distancing in respect to Core HBM variables

Results of the bivariate regression for the surveys of control group indicated that physical distancing is highly correlated with the perceived barrier (OR=*0.64; individuals who perceive barriers to physical distancing are less likely to practice it)* and perceived benefits (OR=*2.683)* of physical distancing. There is no significant correlation between physical distancing and perceived susceptibility and perceived severity of influenza. For the treatment group, physical distancing is highly correlated with perceived susceptibility

(OR=*1.783)* and perceived severity (OR=*1.921)* of disease and the perceived benefits (OR=*3.789)* of physical distancing. There is no significant correlation between physical distancing and the perceived barrier of this behavior.

The multivariate logistic regression for the control group indicates that perceived susceptibility to influenza, perceived barriers and perceived benefits of physical distancing are correlated with physical distancing while the perceived severity of influenza is not quite significant at the .05 level. Multivariate regression results for the treatment group indicated that all HBM variables are correlated with physical distancing, while self-isolation was correlated with perceived susceptibility to influenza and perceived barriers and benefits of self-isolation, but the perceived severity of influenza is not correlated with self-isolation.(Table VI)

The multivariate logistic regression indicates that all the HBM variables are correlated with physical distancing in both control and treatment group, however perceived severity of influenza in control group is not significant at the 0.05 level. The results also indicate that all the HBM variables except perceived benefits of self-isolation are correlated with this intervention in control group. The results for treatment group indicate that all HBM variables are correlated with self-isolation except perceived severity of influenza.(Table VI)

Table VI: Multivariate logistic regression of HBM variables attitudinal variables associated with influenza interventions

	Vaccination				***Self-Isolation***				***Physical distancing***			
	Control Group		***Treatment Group***		***Control Group***		***Treatment Group***		***Control Group***		***Treatment Group***	
	Odds Ratio	***P-Value***	***Odds ratio***	***P- Value***	***Odds ratio***	***P-value***	***Odds ratio***	***P-Value***	***Odds ratio***	***P-Value***	***Odds ratio***	***P-Value***
Perceived Susceptibility:												
Strongly agree, agree, neutral,	*1*		*1*		*1*		*1*		*1*		*1*	
Strongly disagree, disagree	*2.6*	*0.003*	*3.41*	*0.041*	*1.743*	*0.021*	*3.84*	*0.0089*	*1.243*	*0.032*	*1.541*	*0.0118*
Perceived Severity:												
Strongly agree, agree, neutral	*1*		*1*		*1*		*1*		*1*		*1*	
Strongly disagree, disagree	*1.42*	*0.58*	*1.73*	*0.0032***	*2.221*	*0.00079*	*1.523*	*0.3*	*1.426*	*0.0566*	*2.623*	*0.015*
Vaccination Perceived Benefits												
Strongly agree, agree, neutral	*1*		*1*		*n.a.*		*n.a.*		*n.a.*		*n.a.*	
Strongly disagree, disagree	*2.58*	*0.0061*	*2.62*	*0.086*								
Vaccination Perceived Barriers												
Strongly disagree, disagree, neutral	*1*				*n.a.*		*n.a.*		*n.a.*		*n.a.*	
Strongly agree, agree	*0.421*	*0.012*	*0.632*	*0.021*								
Self- Isolation Perceived Benefits												
Strongly agree, agree, neutral	*n.a.*		*n.a*		*1*		*1*		*n.a.*		*n.a.*	
Strongly disagree, disagree					*2.712*	*0.368*	*2.473*	*0.00062*				
Self- Isolation Perceived Barriers												
Strongly disagree, disagree, neutral	*n.a.*		*n.a.*		*1*				*n.a.*		*n.a.*	
Strongly agree, agree					*0.277*	*0.0021*	*0.341*	*0.0469*				
Physical Distancing Perceived Benefit												
Strongly agree, agree, neutral	*n.a.*		*n.a*		*n.a.*		*n.a.*		*1*		*1*	
Strongly disagree, disagree									*2.564*	*0.041*	*4.6*	*0.0056*
Physical Distancing Perceived Barriers												
Strongly disagree, disagree, neutral	*n.a.*		*n.a.*		*n.a.*		*n.a.*		*1*		*1*	
Strongly agree, agree									*0.371*	*0.026*	*0.762*	*0.0036*

Notes:* $p \leq 0.05$,**$p \leq 0.01$,***$p \leq 0.001$. NA (Not Applicable), NS (Not Significant at $p \leq 0.05$)

Gender and Cues to Action Variables

Table VII displays the results of gender and cues to action variables included in the survey. Results shows that participants who live with a member of a group at risk for influenza are more likely (3.226 odds ratio) to receive vaccination and also to apply distance in their physical contacts with others (2.259 odds ratio). The results also indicate that females are more likely to develop social distancing behavior toward influenza and people with past vaccination experience are more likely to get vaccinated in the future.

Perceived Susceptibility of influenza in respect to Cues to Action variables

Our regression results did not indicate significant correlation between perceived susceptibility of influenza and past experience of vaccination. However there is a significant correlation between perceived susceptibility of influenza and living with a member of a high risk group (OR=1.892). (Table VIII)

Table VII: Bivariate logistic regression of Gender and Cues to Action variables associated with influenza interventions

	Vaccination		*Self-Isolation*		*Physical distancing*	
	Odds Ratio	***P-Value***	***Odds Ratio***	***P-Value***	***Odds Ratio***	***P-Value***
Gender						
Male	*n.s*		*1*		*1*	
Female			*0.234*	*0.042*	*0.395*	*0.0095*
Have you ever been vaccinated against influenza in the past?(cues to action)						
Yes	*1*		*n.s.*		*n.s.*	
No	*5.4*	*0.013*				
Does someone with a compromised immune system live in your home?(cues to action)						
Yes	*1*				*1*	
No	*3.226*	*0.036*	*n.s.*		*2.592*	*0.03*

Notes:* p≤0.05,**p≤0.01,***p≤0.001. NA (Not Applicable), NS (Not Significant at p≤0.05)

Table VIII: Bivariate logistic regression of cues to action variables associated with perceived susceptibility of influenza

	Perceived Susceptibility	
	Odds Ratio	***P-Value***
Have you ever been vaccinated against influenza in the past?(cues to action)		
Yes	n.s.	
No		
Does someone with a compromised immune system live in your home?(cues to action)		
Yes	1	
No	1.892	0.0073

Notes:* p≤0.05,**p≤0.01,***p≤0.001. NA (Not Applicable), NS (Not Significant at p≤0.05)

3.4.6. Discussion

The comparison of survey sessions in Table I revealed a significant increase in perceived susceptibility of influenza after the health information session. This result suggests that providing participants with information on their high susceptibility to influenza and various routes of influenza transmission, the virus high potential for transmission and physical susceptibility of influenza, by a specialist could increase the perceived susceptibility to influenza. Also, a significant increase in participants' perceived low barriers of influenza vaccination was observed after the health information session. The specialists provided students with information on Concordia's new policy to vaccinate students, staff and faculty who are or live with a member of high risk group in Concordia's Health Center for free and also the Center's ability to provide others with vaccination services at low cost. The information session did not cause any significant change on the perceived severity of influenza and the perceived benefits of vaccination. The analyses of HBM variables revealed that perceived susceptibility to influenza, perceived benefits and perceived barriers to vaccination are the core predictors of this protective behavior (Table VI). These results suggest that educational programs or information distributions which provide sufficient information to increase individuals' perceived susceptibility toward influenza, and also provide participants with enough information on influenza vaccination, its efficiency, its low potential side effects and availability, could increase the rate of developing this efficient protective behavior.

The result of comparison between sessions (Table IV) also revealed that the participants' perceived benefits of social distancing increased after the information session. The results of multivariate logistic regression (Table VI) demonstrate that perceived susceptibility, perceived barriers and perceived benefits of both self-isolation and social distancing are the significant predictors for these behaviors. These results suggest educational programs which focus on susceptibility to the influenza virus (by focusing on the high probability of the disease transmission via physical contacts) and the perceived benefits and perceived barriers of social distancing (by providing information on university policies to ensure that there are no academic consequences for staying home while sick, i.e., no punishment for missed classes and examinations, turning in assignments late, etc.) will have a higher effect on increasing students self-isolation.

In our study, participants with a history of vaccination against influenza prior to current year (cues to action) were more likely (5.4 odds ratio) to receive vaccination than people with no history of vaccination. Variables such as experience, the level of comfort with the vaccine and developed health beliefs; such as the perceived benefits (with mean of 4.02 for people with history of vaccination) and the perceived barriers (with mean of 2.21 for people with history of vaccination) may be the cause of such behaviors. These results suggest that educational programs which focus on the portion of the population with no history of vaccination could be more helpful to increase the total vaccination rate.

Participants with members of high risk groups in their household (cues to action) also were more likely to develop protective behaviors toward influenza.

Our results show that educational programs and information distribution could be very helpful in changing individual attitudes and beliefs toward influenza, which could in turn lead to developing protective behaviors. Such programs should focus on providing information on perceived benefits of social distancing and vaccination. In addition, we expect to see benefits from policies aimed at reducing the costs of vaccination and increasing accessibility in places such as university-based health centers. In addition, policies to minimize the costs and consequences of missing work and school in order to support self-isolation during outbreaks may be a key to reducing seasonal influenza outbreaks.

3.5. Incorporating Individual Behaviors into Simulation

Students protective behaviors were estimated using the four core domains of the Health Belief Model: perceived susceptibility, perceived severity, perceived benefits and perceived barriers of based on the HBM survey. These variables interact to produce a probability of action for each intervention.

The probabilities of social distancing and vaccination for each individual were incorporated into the simulation as the health-behavior pattern, driven from the standard logistic regression equation expressed in terms of odds ratios.

$$p(behavior) = \frac{OR_0 * \prod OR_i^{x_i}}{1 + OR_0 * \prod OR_i^{x_i}}, \quad i = 1, \dots, 4 \quad (7)$$

Equation 7 gave a value p (behavior) between 0 and 1. A random number was generated based on the probability. Behavior was determined as 'engages in behavior' if the random number > p (behavior), 'does not engage in behavior' otherwise. $i = 1, \ldots, 4$ represents the four HBM domains. OR_i indicates the relative odds ratio of the behavior when the corresponding domain status is 'high' relative to when it is 'low' (correspondence odds ratio of multivariate logistic regression). x_i is a binary variable representing the state of the corresponding HBM domain, with a value of 1 indicating a 'high' state of the HBM domain and a value of 0 indicating a 'low' state. OR_0 functions as a calibration constant by defining the probability of the behavior when all x_i variables are in the 'low' state. Developing a behavior is most likely to have a positive correlation with 'high' state of perceived susceptibility to disease, perceived severity to disease and perceived benefits of the behavior. However developing a behavior is most likely to have a positive correlation with 'low' state of perceived barrier to the behavior.

Since the influenza vaccine contains only the three main strains of the virus, the efficiency of vaccine to prevent infection was estimated to be 87%. Those that were vaccinated and became infected had their infectiousness hazard rate reduced by a factor of 50%, relative to unvaccinated cases. In addition, vaccination reduces the infectious period by one day. (Longini, 2005) we chose to use historical values from the literature rather than the most recent values due to year to year change of vaccination efficiency and also to be able to compare the results of this simulation to other existing simulations.

Social distancing (avoidance of close physical contact) was employed in the model as a reduction in the probability of infection. It was assumed that social distancing reduces both the susceptibility and infectiousness of the population by a certain percentage.

Self-isolation was employed in the model as an option for infectious people. Individuals may decide to go into the self-isolation after developing symptoms. These individuals would be transferred to their normal schedule compartment after the end of the infectious period.

Table IX illustrates a summary of the set of attributes of individuals and information required to build the contact network as well as disease related data.

Table IX: Summery of HBM variables multivariable logistic regression odds ratio for influenza interventions

Interventions	HBM Variables	Odds Ratio	Interventions	HBM Variables	Odds Ratio
Vaccination	*Perceived Susceptibility*	*2.6*	*Vaccination*	*Perceived Susceptibility*	*3.41*
	Perceived Severity			*Perceived Severity*	*1.73*
	Perceived Benefits	*2.58*		*Perceived Benefits*	
	Perceived Barriers	*0.421*		*Perceived Barriers*	*0.632*
Social Distancing	*Perceived Susceptibility*	*1.243*	*Social Distancing*	*Perceived Susceptibility*	*1.541*
	Perceived Severity			*Perceived Severity*	*2.623*
	Perceived Benefits	*2.564*		*Perceived Benefits*	*4.6*
	Perceived Barriers	*0.371*		*Perceived Barriers*	*0.762*

*p value< 0.05

Table X: Cumulative probabilities of frequency for behavior combinations (Control Group)

Combinations	Perceived Susceptibility	Perceived Severity	Perceived Vaccination Benefit	Perceived Vaccination Barrier	Perceived Physical distancing Benefit	Perceived Physical distancing Barrier	Perceived Self-Isolation Benefit	Perceived Self-Isolation Barrier	Probability
1	0	0	0	1	0	1	0	1	3.1
2	0	0	0	1	1	0	0	1	4.6
3	0	0	0	1	1	1	0	1	7.7
4	0	0	1	0	0	1	0	0	9.2
5	0	0	1	0	1	0	0	0	13.8
6	0	0	1	0	1	1	0	0	16.9
7	0	0	1	1	0	0	0	1	18.5
8	0	0	1	1	1	0	1	1	20.0
9	0	0	1	1	1	1	1	1	21.5
10	0	1	0	0	0	1	0	0	23.1
11	0	1	0	0	1	0	1	0	26.2
12	0	1	0	0	1	1	0	0	27.7
13	0	1	0	1	1	0	0	1	29.2
14	0	1	0	1	1	0	1	1	30.8
15	0	1	0	1	1	1	0	1	33.8
16	0	1	1	0	0	0	1	0	35.4
17	0	1	1	0	1	0	0	0	36.9
18	0	1	1	0	1	0	1	0	38.5
19	0	1	1	0	1	1	0	0	40.0
20	0	1	1	1	0	1	1	1	41.5
21	0	1	1	1	1	0	0	1	46.2
22	0	1	1	1	1	0	1	1	49.2
23	0	1	1	1	1	1	0	1	50.8
24	0	1	1	1	1	1	1	1	53.8
25	1	0	0	0	0	0	1	0	55.4
26	1	0	0	0	1	0	0	0	56.9
27	1	0	0	1	1	1	0	1	58.5
28	1	0	1	0	0	1	1	0	60.0

29	1	0	1	0	1	1	0	0	61.5
30	1	0	1	1	0	1	0	1	63.1
31	1	1	0	0	1	1	0	0	66.2
32	1	1	0	1	1	0	0	1	69.2
33	1	1	0	1	1	1	0	1	70.8
34	1	1	0	1	1	1	1	1	73.8
35	1	1	1	0	1	0	0	0	75.4
36	1	1	1	0	1	1	1	0	78.5
37	1	1	1	1	0	0	0	1	80.0
38	1	1	1	1	1	0	0	1	83.1
39	1	1	1	1	1	0	1	1	87.7
40	1	1	1	1	1	1	0	1	95.4
41	1	1	1	1	1	1	1	1	100.0

Table XI: Cumulative probabilities of frequency for behavior combinations (Treatment Group)

Combinations	Perceived Susceptibility	Perceived Severity	Perceived Vaccination Benefit	Perceived Vaccination Barrier	Perceived Physical distancing Benefit	Perceived Physical distancing Barrier	Perceived Self-Isolation Benefit	Perceived Self-Isolation Barrier	Probability
1	0	0	0	0	0	0	0	0	.7
2	0	0	0	0	0	1	1	0	1.4
3	0	0	0	1	1	1	1	1	2.2
4	0	1	0	0	0	0	1	1	2.9
5	0	1	0	1	1	1	1	1	5.0
6	0	1	1	0	1	1	1	1	6.5
7	0	1	1	1	1	1	1	1	7.2
8	1	0	0	1	1	1	1	1	7.9
9	1	0	1	0	0	1	1	1	8.6
10	1	0	1	1	1	1	1	1	10.1
11	1	1	0	0	1	1	1	0	10.8
12	1	1	0	0	1	1	1	1	14.4
13	1	1	0	1	0	1	0	0	15.1

14	1	1	0	1	0	1	1	1	17.3
15	1	1	0	1	1	1	1	0	19.4
16	1	1	0	1	1	1	1	1	45.3
17	1	1	1	0	1	1	1	1	48.2
18	1	1	1	1	0	0	1	1	48.9
19	1	1	1	1	0	1	1	0	49.6
20	1	1	1	1	0	1	1	1	52.5
21	1	1	1	1	1	1	0	1	54.0
22	1	1	1	1	1	1	1	0	56.1
23	1	1	1	1	1	1	1	1	100.0

The multivariate logistic model represents behavioral decisions as a function of a set of states of the HBM constructs. At the start of simulation a random number was generated for each individual based on the probabilities derived from the survey results. (Table X and XI). The probabilities of three behaviors: vaccination, social distancing and isolation, were calculated based on the behavior states and odds ratio derived from survey.

3.6. Contact Network

The flow of students through a university involved a modest number of decision points. Therefore, students were assigned to have hypothetical specific daily activities .To acquire data on students' activities on campus, a questionnaire survey was conducted. A total 260 valid questionnaires were collected from undergraduate engineering students at Concordia University. These data were inputted into the simulation database to build student activity patterns. According to the collected data students were more likely to spend their free time on campus in the library, laboratories, student lounge and gym .Also some preferred to spend their free time off campus. Whenever agent finished a scheduled class it was given the option to select its next location based on these activity patterns. Each location in the simulation was described by a matrix of seating orders. Students were assigned to an element of the matrix randomly upon their arrival to a location. For susceptible individuals, all the nearby elements which were within the attack radius were monitored for infectious contacts and once that person decided to leave the location the probability of infection were calculated. If infectious contacts were effective the health status was changed to exposed-noninfectious. Once a susceptible individual left campus the probability that s/he came back to school exposed to the virus was calculated based on duration and the average contacts that an individual might have in the general community or household following the assumptions in Haber et al. study (Haber et al., 2007)

Table XII Summary of information used in simulation

Individual Attributes		System Information	
Social	*Student ID*	*Locations*	*Geography*
	Class Schedules	*Disease*	*Infectivity Index*
	Activity Schedules		*Vaccination Efficiency*
Behavior	*HBM Variables*		*Social Distancing Efficiency*
	Vaccination Probability		*Infectious Period Distribution*
	Social Distancing Probability		*Exposed Period Distribution*
	Self-Isolation Probability		*Symptomatic and Asymptomatic Probability*
Disease	*Exposed Period*		*Asymptomatic case Infectivity*
	Infectious Period		

3.7 Simulation Structure

We used Arena Simulation Software 13.9 to build our model. In this section we discuss the compartments of the simulation.

Station Information:

In this section stations' information, related to each location (classrooms, laboratories, library, student lounge), such as station ID, station's seating arrangements and station's capacity was incorporated into simulation from excel files. (Figure IV)

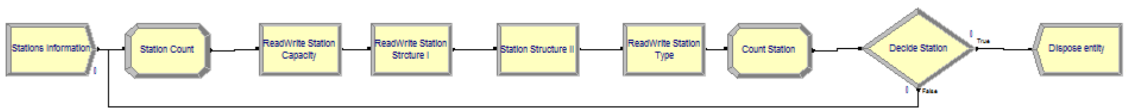


Figure IV: Simulation Capture of stations information

Individual Attributes:

In this section student attributes such as student ID, the probability of developing protective behaviors (vaccination physical distancing and isolation), students course schedules, disease attributes such as latent period and infectious period, etc. were incorporated into the simulation. (Figure V)

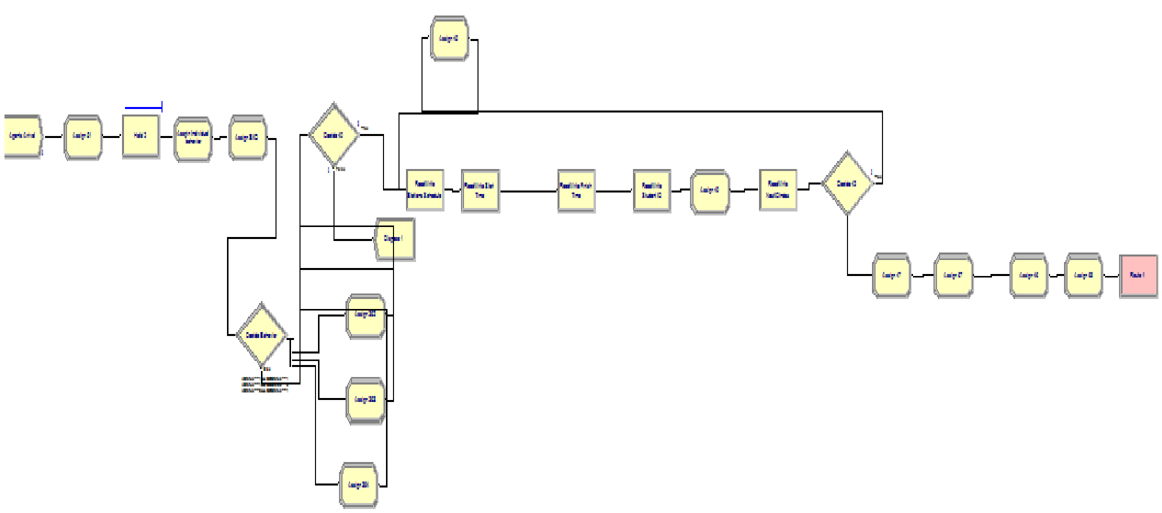


Figure V: Simulation Capture of individual attributes

Decision Station:

Decision station was developed to regulate agents' flow in simulation. Once an agent finishes its activity. It enters decision station to be sent to its next activity. If the next activity is a scheduled class in less than 20 minutes, agent is hold in decision station until the activity starts. If the next scheduled class is in more than 20 minutes, agent is sent to one of the following stations: Home, Out, Library , Laboratory or Student Lounge, based on the probabilities driven from survey. (Figure VI)

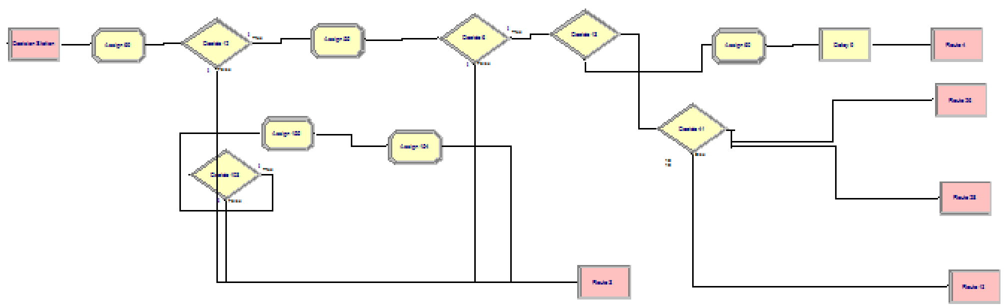


Figure VI: Simulation Capture of Decision Station

Classroom, Laboratories. Library and Student Lounge

Once an agent enters to one of the following stations: Classroom, Laboratories. Library and Student Lounge, it is assigned to a seat randomly. Disease state of agents assigned to seats within the influenza attack distance is checked at arrival and departure of a susceptible agent and probability of infection is calculated based on attack duration and hazard rates. (Figure VII and VIII)

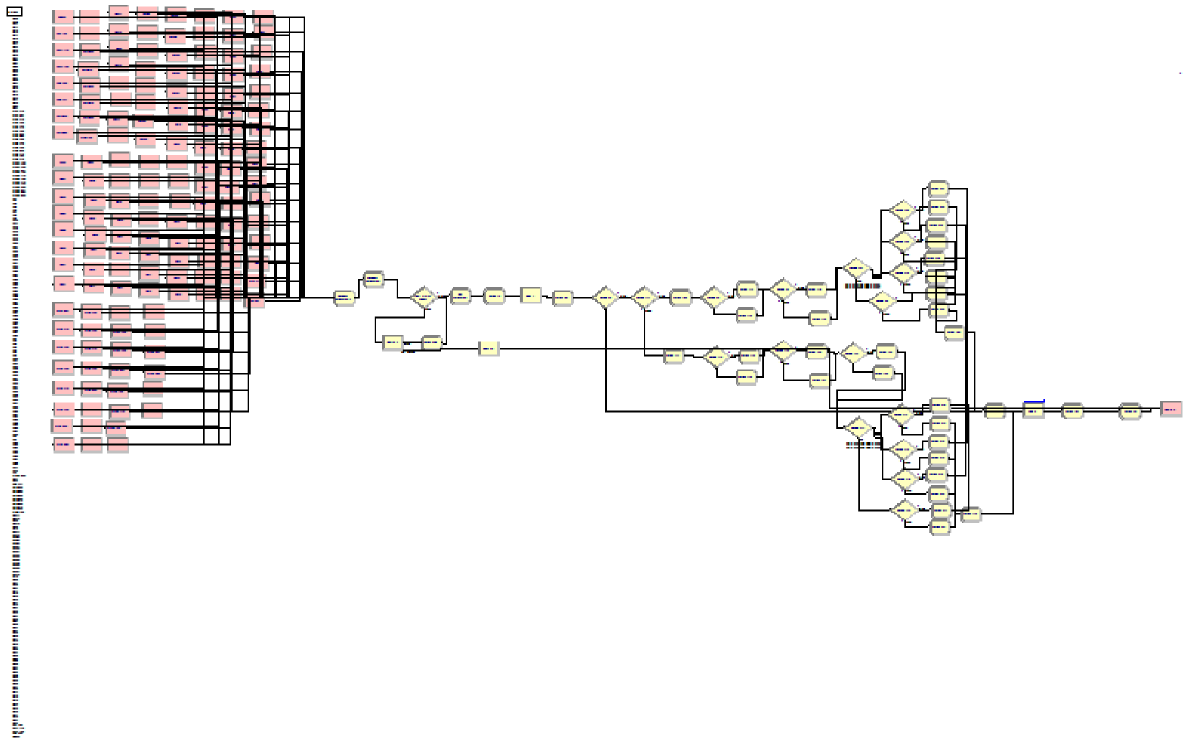


Figure VII: Simulation Capture of Classrooms and laboratories

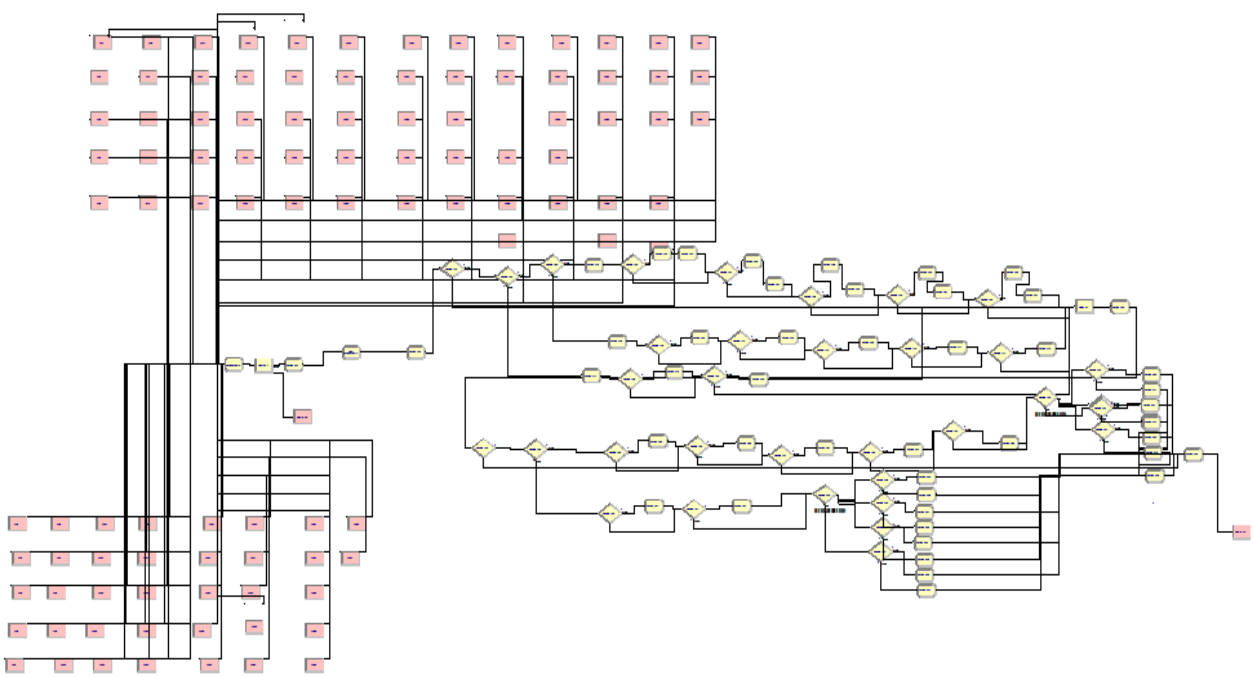


Figure VIII: Simulation Capture of Library and Student Lounge

Home Station:

Home Station represents the household of students. In this station, disease state of agents is checked. If agent is in latent or infectious state and the latent or infectious period is passed, disease state is changed to Infectious-Asymptomatic/ Infectious-Symptomatic or Recovered respectively. If agent disease state is Susceptible the probability of infection is calculated. (Figure IX)

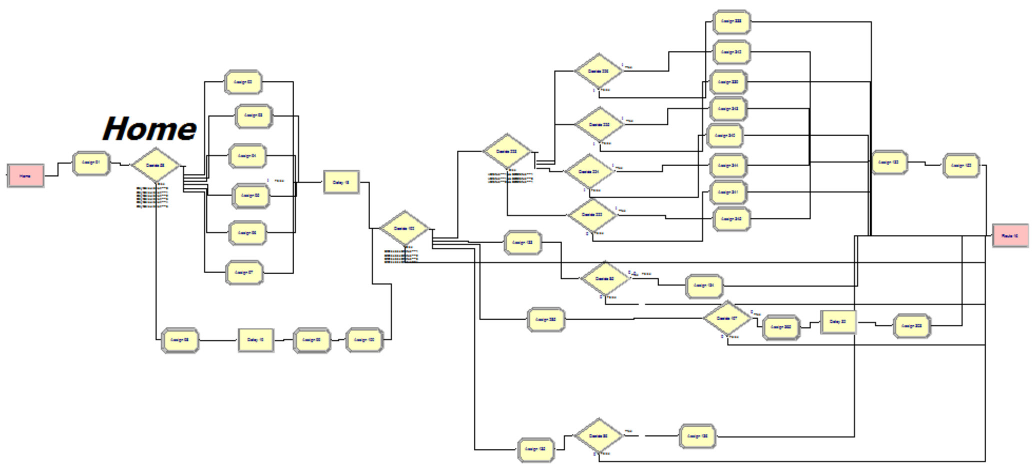


Figure IX: Simulation Capture of Home Station

Community

Home Station represents the community. If agent disease state is Susceptible the probability of infection is calculated. (Figure X)

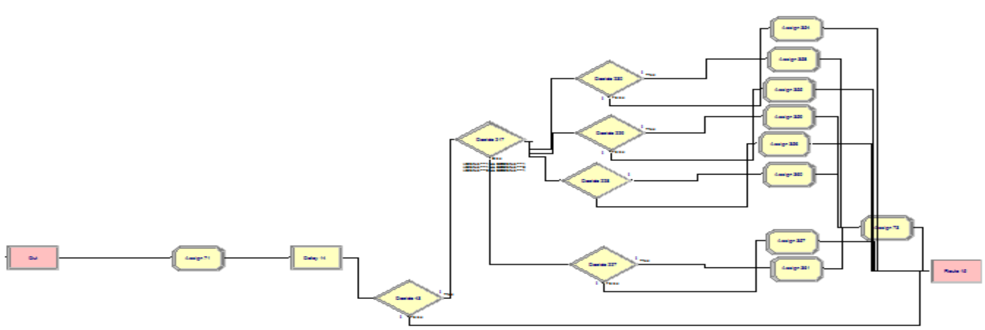


Figure X: Simulation Capture of community

4 Results

In this chapter, we present the numerical results of our analysis in three sections. First we validate our simulation by comparing results of our disease spread simulation such as attack rate, peak period and R_0 to results of similar studies. Then we present the result of two pre-defined scenarios. First scenario illustrates the spread of influenza within the target population using the odds ratios driven from control group and second scenario illustrates the spread of influenza within the target population using the odds ratios driven from treatment group.

4.1. Model Validation

The baseline scenario was defined without consideration of individual protective behaviors. 33% of individuals who became infected withdrew from their daily activity schedules once they got sick, and remained at home through their symptomatic period (Longini, 2004). To validate our simulation two approaches were considered. First, the peak time of the outbreak in the university was obtained from the curve of the number of infected individuals per day in the system with the baseline scenario of 4864 susceptible students. (Figure XI) The number of infection and the attack rates of influenza with 95 percent confidence intervals for the baseline scenario for 20 simulations are shown in Table XIII. The peak infection rate occurred from days 24 to 30 after the start of the outbreak with the average rate of 165 new cases per day. By the day when the peak new case rate occurs, the cumulative number of infections reaches the average of 1813.6. The simulation was run out to day 60, by which time the average of 2735 people had been infected and the overall attack rate was more than 50% (in a population with 4884 susceptible individuals and no protective behaviors) These results were consistent with the study of Yang and Atkinsonin a characteristically similar population with the peak time between 20 and 25 days and overall attack rate of more than 50%. Second, the value of R_0, (defined the number of secondary infection of individuals in a susceptible population by the introduction of a single infectious individual) (Diekmann, Heesterbeek, & Metz, 1990), was estimated by calculating the number of secondary infections after entering only one infected individual in the simulation. In the literature the value of R_0 of influenza was estimated from 0.9 to 2.1 with a mean of 1.3 (Chowell Miller, & Viboud, 2007; Ferguson et al., 2005; Mills, Robins, & Lipsitch, 2004). In our simulation the value of R_0 after 20 simulations was estimated to be 1.45.

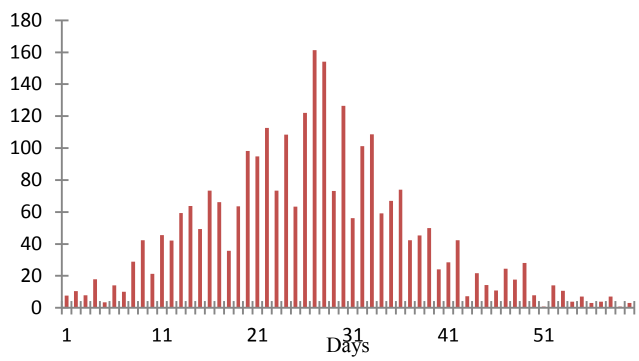


Figure XI: Number of New infection per day

4.2. Health-related protective behaviors

The second scenario included the HBM variables, which were used to calculate the probability of developing the protective behaviors (social distancing and vaccination) for each agent in the system and also the probability of self-isolation. It should be noted that individuals who applied social distancing in their contacts with others when they were sick reduced the probability of infection for others. An average of 1614 ± 11 cases of influenza was observed with the attack rate of approximately 34 percent. We run the simulations for 70 days. The peak of the outbreak was also delayed by an average of 6 days and the average rate of new cases in the peak period was 123 per day. Of the average of 488 ± 9 people who developed both protective behaviors only 18 ±3 did not escape infection. Of 603± 8 individuals who just vaccinated themselves against influenza 62 ±3 got sick with flu and from 628 ± 11 students who just applied social distancing on their contacts with others 289 ± 3 still got sick with flu. The self-initiated protective behaviors of population toward influenza were able to reduce the attack rate by more than 16 percent. 483 ± 6 people preferred to stay at home when they were sick with flu. The difference between the protection efficiency of vaccination and social distancing explains the significant difference between the rate of people who got infected even though they were vaccinated and those who applied social distancing in their contacts. An average of Total 1721 (approximately 35 %) of students developed at least one self-initiated protective behavior toward influenza. Therefore an average of 75% percent of people who got sick during flu season, were the people with no self-initiated protective behavior toward influenza. These results illustrate that considering the current state of individuals perceived susceptibility and severity of influenza along with the perceived benefits and perceived barriers of interventions could have a significant effect on the attack rate of influenza within a university.

4.3. Educational Program

The third scenario included the protective behaviors that individuals developed, after receiving a treatment in the form of an educational program designed to increase students' willingness to get vaccinated or apply social distancing in their social contacts with others in case of an influenza outbreak in the university. The multivariable logistic regression of HBM variables provided us with individual health-related activities during a flu season. After 20 simulation runs for this scenario, the result illustrated that only an average of 987 ± 6 (attack rate of 21 %) , cases of influenza occurred. Of the 598 ± 12 people (on average) who developed both protective behaviors only 21 ± 5 did not escape the infection. Of the 1013±22 whom just vaccinated themselves against influenza 95±4 were sick with flu and from 928±16 students who just applied social distancing on their contacts with others, only 273 ±9 were sick with flu. 283 ± 6 people preferred to stay at home when they were sick with flu. Total attack rate of influenza decreased by approximately 12 after the educational program which led to a 20% percent increase in number of vaccination and 42% increase in social distancing behavior. The peak of the outbreak was shifted by an average of 8 days and the total number of new infected cases in the peak of the outbreak decreased by 34 percent. The summary of results extracted from simulations for both scenarios is described in table XIV.

Table XIII : Summery of simulation results

Statistics	Baseline Scenario		Control Scenario		Treatment Scenario	
	N	95 %CI	N	95% CI	N	95 % CI
Total Cases	2735.17	±31.61	1614.61	± 11.34	987.12	±16.35
Peak Cases	165.44		123.31		87.5	
Peak Day	20-25		26-34		37-45	
Self-Isolation Cases	896.31	±17.81	483.41	±9.21	383.41	±11.34

Table XIV: Comparisons of control and treatment scenarios

Statistics	Control Scenario		Treatment Scenario	
	N	95% CI	N	95 % CI
Total Number of Hybrid Behaviors	488	± 9	598	± 12
Total Infected Cases with Hybrid Behaviors	18	±4	21	± 5
Total Number of Vaccination	603	± 8	1013	±22
Total Infected Cases for vaccination	62	±3	95	±4
Total Number of Social Distancing	628	± 11	928	±16
Total Number of Infected Cases with social distancing	289	±7	273	±9

5. Conclusion

This agent based simulation model is the first of its kind to incorporate the effect of instinctive protective behaviors that individuals develop on the spread of an infectious disease within a structured population. The evaluation of results indicated that such behaviors were successful in controlling the outbreak in a high contact rate place such as a university by a significant decrease on the attack rate (approximately 17%) of disease among the population and an observable moderate peak of outbreak by a 25 % reduction in the peak number of cases. This result highlights the importance of considering self-initiated behaviors that individuals develop to protect themselves in case of an outbreak. It should be noted that both protective behaviors (social distancing and vaccination) are dependent on each other, which may explain the enhancing effect of these behaviors on controlling the outbreak, compared to other studies which have incorporated influenza interventions as independent parameters. (M. J. Haber, 2007) (T. Das, 2008) (Longini, 2004) The effect of social distancing on controlling the transmission is explained by characteristics of influenza virus transmission as an airborne virus, individuals have to be within a certain distance of each other for a contact to be effective. The output of our simulations also provide evidence that, along with vaccination, non-pharmaceutical interventions such as social distancing are able to control the outbreak of disease , which could help individuals with perceived high barriers of vaccination to protect themselves against influenza. The simulation also provides significant evidence for the effect of an HBM theory-based educational program to increase the rate of applying the target interventions among populations (vaccination by 22 % percent and social distancing by 41%) and consequently to control the outbreak. Although the probability that a person develops a protective behavior cannot be entirely controlled, studies have demonstrated that providing information which targets different aspects of disease and its interventions could have a significant effect on such probabilities.

6. Future Work

The modeling approach used to simulate the transmission of influenza provides a novel representation of the real world by considering aspects of both social and health related individual behavior patterns, which could be applied to different circumstances of other infectious diseases or other population structures. Although a university environment was defined as the target population in this simulation, the model could be applied to larger case studies, provided sufficient data resources for both individual activity patterns and health behaviors (by conducting HBM on populations with more characteristics diversity such as age, race and education level). The advantages of this study include understanding individual behavior and its effect on the spread of disease and efficiency of educational programs to shape behavior. Some of the characteristics of this model such as the massive data collection required to develop the social activity patterns, the uncertainty of influenza transmission probability calculation and the limitations of HBM to explore other factors that might influence people decision making process (for example fear and diversity of population) could lessen the efficiency of this simulation on larger case studies. Instead, lessons learned from models at this scale may need to be generalized for larger populations. Another future direction may be the implication of probabilistic risk assessment (PRA) to calculate the risk of disease transmission for different educational programs. Finally the estimation of real costs for each intervention, the cost of loss work for students in case of infection and cost of educational programs could provide us with cost-effectiveness analysis of educational programs and interventions , which is another improvement that may be followed in the future, which of course depends on the availability of data.

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Appendix I: Binary Logistic Regression

The logistic model has the form of predictor Y is:

$$\ln\left(\frac{\pi}{1-\pi}\right) = \log(\text{odds}) = \alpha + \beta x,$$

where π is the probability of the outcome of interest, under variable Y, α is the Y intercept, and β is the slope parameter.

Odds of an Event is:

$$\text{ODDS} = P\ (A) / 1 - P\ (A)$$

where P(A) is the probability of event A.

For instance if the odds of event A are 4, this means that A is 4 times more likely to happen than not happen.

This concept could be applied to a case of the ratio of odds of an event for one group relative to the odds of the same event for another group. The odds ratio of an event for two groups can be expressed as follows:

$$\frac{P(A/Group\ 1)\ /\ [1 - P(A/Group1)]}{P(A/Group\ 2)\ /\ [1 - P(A/Group2)]}$$

Therefore, the regression coefficient β, calculated in logistic regression is the estimated increase in the log odds of the outcome per unit increase in the value of the predictor variable. In other words, the exponential function of the regression coefficient (e^{β}) is the odds ratio associated with a one-unit increase in the predictor variable.

The odds ratio is used to determine whether a particular predictor is a risk factor for a particular outcome, and to compare the magnitude of various risk factors for that outcome.

OR= 1: means that predictor variable does not affect odds of outcome

OR>1: means that the predictor variable is associated with higher odds of outcome

OR<1 : means that the predictor variable is associated with lower odds of outcome

If the dependent variable in a logistic regression results in two mutually exclusive outcomes, for example, pass or fail, or as in our model to develop a behavior or not, a binary logistic regression would be used to describe the outcome. In this study the odds ratio were used to determine whether the state of each HBM variable (binary predictor as 0 for low and 1 for high perceived variable) is associated (correlated) with developing protective behaviors (binary outcome).

The 95% confidence intervals (CI) were also used in the model to estimate the precision of the odds ratios. A large CI indicates a low level of precision of the odds ratio, whereas a small CI indicates a higher precision of the odds ratio.

Appendix II: Multivariate Logistic Regression

If π(x) represent the probability of an event that depends on n independent variables, then, using formulation for modeling the probability, we have:

$$\pi(x) = \frac{e^{\beta_0+\beta_1 X_1+\beta_2 X_2+\cdots\beta_n X_n}}{1+e^{\beta_0+\beta_1 X_1+\beta_2 X_2+\cdots\beta_n X_n}}$$

The corresponding logistic function from this, we calculate (letting X represent the whole set of variables X_1, X2, . . . , X_p):

$$Logit[\pi(x)] = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots \beta_n X_n$$

In the calculated multivariate logistic regression for our model, each estimated coefficient is the expected change in the log odds of engaging in the protective behavior, if the corresponding HBM variable state changes from low to high, holding the other predictor variables constant. The value of β_0 illustrates the likelihood of engaging in preventive behaviors among those who perceived all four variables lowly.

Appendix III: Survey

Gender					
O Female	O Male				
Status					
O Undergraduate Student	O Graduate Student	O Faculty	O Staff	O Other	
Faculty					
O ENCS	O JMSB	O Fine Arts	O Arts & Science	O Other	

	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
If I get the influenza virus, I will get sick.	O	O	O	O	O
If I get the influenza virus, it will disrupt my studies.	O	O	O	O	O
If I get the influenza virus, others in my home will get sick.	O	O	O	O	O
I am at risk of getting the influenza virus by going to the university.	O	O	O	O	O
My family members are at risk of getting the influenza virus.	O	O	O	O	O
I feel knowledgeable about my risk of getting the influenza virus.	O	O	O	O	O
If I get the influenza vaccine, I will not get sick from the influenza virus.	O	O	O	O	O

If I get the influenza vaccine, I will have side effects.	○	○	○	○	○
It is inconvenient to get the influenza vaccine.	○	○	○	○	○
I will recover faster if I rest at home as soon as influenza symptoms develop.	○	○	○	○	○
Staying at home when I am sick has a negative effect on my studies.	○	○	○	○	○
My professors do not consider illness as an excusable reason for absence.	○	○	○	○	○
Avoiding crowded places reduces my likelihood of catching influenza.	○	○	○	○	○
Avoiding physical contact with sick people reduces my likelihood of catching influenza.	○	○	○	○	○
It is difficult to avoid close physical contact with my friends when I am sick.	○	○	○	○	○
It is difficult to avoid crowded places at the university.	○	○	○	○	○
My knowledge about influenza and its interventions is sufficient.	○	○	○	○	○
I will use medication if I get the influenza virus.	○	○	○	○	○

Where do you prefer to spend time when you have a gap between lectures?

	Never	Sometimes	Often	Very Often
Off Campus	○	○	○	○
Le Gym	○	○	○	○
Library	○	○	○	○
Laboratories	○	○	○	○
Student Lounge in Hall Building	○	○	○	○
Other (Please specify):	○	○	○	○

How often do the following resources provide you with information about influenza?

	Never	Sometimes	Often	Very Often
TV	○	○	○	○
Newspaper	○	○	○	○
Family member or friend	○	○	○	○
Pharmacist	○	○	○	○
Nurse	○	○	○	○
Posters around university	○	○	○	○
Internet	○	○	○	○
Other (Please specify):	○	○	○	○

How likely are you to use the following to prevent influenza?

	Very Unlikely	Unlikely	Likely	Very Likely
Vaccine	O	O	O	O
Avoiding physical contact	O	O	O	O
Using masks	O	O	O	O
Using hand sanitizer	O	O	O	O
Antiviral drugs	O	O	O	O
Other (Please specify):	O	O	O	O

Have you been vaccinated against influenza this year?

O Yes O No

Have you ever been vaccinated against influenza?

O Yes O No

Does someone with a compromised immune system live in your home (e.g., infants, elderly, pregnant women)? O Yes O No